Hearing Research 317 (2014) 23–32

Contents lists available at ScienceDirect

Hearing Research

journal homepage: www.elsevier.com/locate/heares

Research paper

Response to best-frequency tone bursts in the ventral cochlear nucleus is governed by ordered inter-spike interval statistics

M.C.M. Wright [a], [*], I.M. Winter [c], J.J. Forster [b], S. Bleeck [a]

[a] Institute of Sound and Vibration Research, University of Southampton, Southampton SO17 1BJ, UK
[b] Mathematical Sciences, University of Southampton, Southampton SO17 1BJ, UK
[c] Centre for the Neural Basis of Hearing, The Physiological Laboratory, Downing Street, Cambridge CB2 3EG, UK

ARTICLE INFO

Article history:
Received 14 December 2013
Received in revised form
31 July 2014
Accepted 11 September 2014
Available online 28 September 2014

ABSTRACT

The spike trains generated by short constant-amplitude constant-frequency tone bursts in the ventral cochlear nucleus of the anaesthetised guinea pig are examined. Spikes are grouped according to the order in which they occur following the onset of the stimulus. It is found that successive inter-spike intervals have low statistical dependence according to information-theoretic measures. This is in contrast to previous observations with long-duration tone bursts in the cat dorsal and posteroventral cochlear nuclei and lateral superior olive, where it was found that long intervals tended to be followed by shorter ones and vice versa. The interval distributions can also be reasonably modelled by a shifted Gamma distribution parameterised by the dead-time and the mean and coefficient of variation of the dead-time corrected ISI distribution. Knowledge of those three parameters for each interval is sufficient to determine the peri-stimulus time histogram and the regularity measures used to classify these neurons.

1. Introduction

The response of neurons in the ventral cochlear nucleus (VCN) to constant-amplitude constant-frequency tone bursts is of interest for two reasons. Firstly, the resultant spike train rasters are used to characterise and classify unit types (Blackburn and Sachs, 1989), by deriving from them the peri-stimulus time histogram (PSTH) and the regularity (Young et al., 1988; Wright et al., 2011), and relating the observed variety of response to the variety in their morphology (e.g. Bourk, 1976; Rhode and Smith, 1986; Blackburn and Sachs, 1989; Winter and Palmer, 1990). Secondly, such inputs represent the simplest inputs to which these neurons respond, and therefore offer the simplest environment in which to study the relationship between input and output (we exclude the case of phase-locking neurons that respond directly to the oscillations that make up the stimulus tone burst and examine only those that respond only to the envelope of the stimulus). In this article we examine the structure of responses to such tone bursts as a prelude to considering responses to more complex and realistic stimuli. We focus particularly on the inter-spike intervals (ISIs), but rather than studying the ensemble of all ISIs in the raster (known as the first-order interval, Winter et al., 2001) we group ISIs according to the order in which they occurred in their respective spike trains.

Goldberg and Greenwood (1966) studied the spike trains generated by long-duration stimuli, including tone bursts, in the cat dorsal and posteroventral cochlear nuclei, and found that long intervals were more likely to be followed by short intervals and vice versa for these neurons. Johnson et al. (1986) studied the spike trains generated by long-duration tone bursts in the cat lateral superior olive (LSO) and found equivalent results. Avila-Akerberg and Chacron (2011) surveyed this and other cases, not restricted to auditory systems, where long ISIs tended to be followed by short ones and vice versa, indicating in each case that successive ISIs were statistically dependant. Avila-Akerberg and Chacron (2011) referred to such ISI sequences as nonrenewal processes and classified the cases studied according to the sign of ISI serial correlation coefficients. In many of the studies they surveyed spike trains were either stationary, having arisen from spontaneous activity, or quasi-stationary, having been evoked by such long stimuli that the adaptation effects at the onset of the stimulus formed only a small proportion of the ISIs. Both the auditory cases mentioned above were quasi-stationary in this sense.

Renewal processes are, by definition, stationary since they consist of events separated by times that are independent and

---

[*] Corresponding author. Tel.: +44 23 8059 2153.
E-mail address: mcmw@isvr.soton.ac.uk (M.C.M. Wright).

http://dx.doi.org/10.1016/j.heares.2014.09.006
0378-5955/© 2014 Elsevier B.V. All rights reserved.

identically distributed. Stationary nonrenewal processes can retain identical distributions without being independent, and this appears to be the case for the studies surveyed by Avila-Akerberg and Chacron (2011). Consider the converse: a process where successive ISIs are statistically independent but their distributions change so that their mean value increases with time. Such a process would be nonrenewal and nonstationary but independent. It would show the opposite behaviour to that observed by Goldberg and Greenwood (1966) and Johnson et al. (1986) because longer-than-average intervals would tend to come from later in the spike train, and therefore be more likely to be followed by other longer-than-average intervals and vice versa. In the present article we show that this is approximately the case for VCN neurons responding to short tone bursts. Specifically we use information-theoretic measures to show that statistical dependence between successive ISIs in these adapting responses is present but small. We also find that the distribution of ISIs for a particular interval number is, after a dead-time, unimodal and can be reasonably modelled by a shifted Gamma distribution.

It is further shown that under the assumption that subsequent ISIs are statistically independent then both the PSTH and the regularity measurements can be reconstructed from the distributions of the ISIs. It is demonstrated that although this assumption is not perfectly satisfied in VCN neurons with constant-amplitude tone burst stimulus, the dependence is small enough that it can be neglected and that reconstructed PSTHs and regularities correspond well to the directly measured versions. Since the ISI distributions can be characterised by three parameters this implies that all the information necessary to determine the response of the neuron to a tone burst can be obtained from three numbers per spike, namely the dead-time and dead-time corrected mean and coefficient of variation (CV) of the distribution of the ISI preceding that spike.

2. Materials and methods

2.1. Electrophysiological recordings

All physiological recordings were obtained from the cochlear nucleus of the urethane anaesthetised guinea pig (*Cavia porcellus*). The procedures are described in detail elsewhere (Bleeck et al., 2006). We measured 2562 extracellular single unit responses from 1433 units in the ventral cochlear nucleus over a period of 52 months. These recordings were performed for the purpose of standard unit classification and were not specifically collected for this study. No attempt was made to systematically sample the VCN. All experiments were carried out under the terms and conditions of the project license at the time issued by the United Kingdom Home Office to the second author.

Spike rasters were obtained for all units by presenting 50 ms tone bursts (5 ms rise/fall time and randomised starting phase) at the unit's best frequency (BF) at 20 dB and at 50 dB (in a subset of neurons) above its threshold. BF was manually determined in an audio–visual technique. Stimuli were repeated every 250 ms for a total of 250 repeats ('runs'). Spontaneous spike rates were also measured for each unit for 10 s in the absence of controlled acoustic stimulation.

2.2. Data selection

Each raster plot was examined by eye and those showing signs of measurement problems such as sudden changes in the pattern of discharge rates during the measurement window were eliminated, as were any showing evidence of phase locking in the ISI histograms (see below), and only neurons that produced at least one interval in each run were included. First spike latency (FSL) was automatically calculated using the method of Chase and Young (2007). This calculates the probability that the observed spike would have been caused by the (previously measured) level of spontaneous activity for each time. The first time when this probability falls below 10^{-6} was chosen by Chase & Young as the latency. Applying this criterion to the spike trains considered here failed to include some spikes that on visual inspection belonged to the first spike cluster in the data set. Choosing the FSL to be 0.3 ms before the time indicated by Chase & Young's method gave results that accorded with visual inspection. We further omitted all runs that had a spike up to 1 ms before this calculated latency, because in these runs the neuron might have been in its refractory state when the stimulus arrived. After excluding unsuitable units, we were left with 784 different units tested at 20 dB of which 757 units were also measured at 50 dB, totalling 1541 measurements.

3. Theory and calculations

All calculations were made using MATLAB and its Statistics Toolbox (Mathworks, 2013).

3.1. Unit classification

The PSTH of each raster was formed using a bin width of 0.1 ms. The PSTH was normalised to show the probability density function of a spike occurring at a given time. The regularity arising from each raster was also calculated from the same spike train data by the methods of Young et al. (1988). Response types at both stimulus levels were classified by the second author according to existing classification schemes (Blackburn and Sachs, 1989; Winter and Palmer, 1995) into one of the following disjoint classes: 277 CS (Sustained Chopper); 455 CT (Transient Chopper); 26 CL (Long-mode Chopper); 209 PN (Primary with Notch); 90 PL (Primary-Like); 148 ON (Onset); 69 OC (Onset Chopper). Another 267 units that were not readily classified using these schemes were termed Unusual (UN) but were not excluded.

3.2. Independence analysis

Formally establishing independence requires one to prove a negative – the absence of any behaviour characteristic of statistical dependence. The size of data sets that are possible ($\leq$250 pairs per interval number per unit) make this difficult since any such behaviour would be hard to distinguish from chance, and we make no claim to have proved independence. Instead we looked for evidence that any such dependence is small.

Johnson et al. (1986) examined the dependence of successive intervals in the LSO by forming conditional means, whereby every ISI is paired with its successor and all pairs for a particular measurement were binned according to the value of the first ISI. The means of the succeeding ISIs in each bin are then plotted against the bin centres, under the assumption that if all intervals are independent of their predecessors each mean should be equal to the mean of the whole sample. This will be true when the ordered intervals are all identically distributed but, as will be shown below, this is not the case for the spike trains considered here. With an adapting neuron intervals get longer as the stimulus proceeds, so long intervals are more likely to be followed by long intervals regardless of dependence or independence (the opposite trend to that observed by Johnson et al., 1986) as discussed in the Introduction. This could be corrected by scaling the ordered intervals so that they all had the same distribution. Johnson et al. (1986) computed error bounds for each bin and counted the number of bins for which the observed conditional mean lay outside them. This proved impractical with our data because shorter stimuli were used meaning that fewer